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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,342	BRANDS, RUDI	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 7-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2 and 7-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2 and 7-26 are pending.

Reopen

This is reopen prosecution because after reconsidering the claimed invention, new grounds of rejections are requested for the record of the prosecution. Office apologize any inconveniency that brought by this reopen practice.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2 and 7-26 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (Scale-Up of Suspension and Anchorage-Dependent Animal Cells in Basic Cell Culture Protocols, Edited by Pollard et al. Humana Press Inc., 1997, pp.59-75), and Pollard (Basic Cell Culture Protocols, Edited by Pollard et al. Humana Press Inc., 1997, Step 14-20 on page 3 and Section 3.2 on page 4-5) on the same ground as stated in the previous Office Action.

Applicants traverse the rejection and submit that examiner oversimplify the presently claimed invention only as a section b) of claim 1. The sections c) and d), as well as sections of a), e), and f) are all ignored.

Applicants' argument has been respectfully considered; however, it is not persuasive.

Claim 1 recites:

A method for the preparation of cells for use in the production of at least one biological, said method being discontinuous and comprising:

a) culturing cells from a preproduction batch,

b) dividing the cells of the preproduction batch into a first part and a second part,

c) employing said first part for the preparation of at least one production batch for production of at least one biological,

d) employing said second part as a seed for the preparation of at least one subsequent preproduction batch,

e) optionally culturing the cells of the subsequent preproduction batch to obtain a great cell population,

f) optionally repeating b) to e), using the cell of the subsequent preproduction batch of d) or e) for the preproduction batch of b).

In the response to the Office Action filed on December 20, 2002, Applicant argues that Applicant divides the cells of preproduction batch into two separate parts, one part for a production batch or batches and a second part for seed or a subsequent preproduction batch or batches. This division is not taught or suggested in the cited prior art documents by Griffith et al. Applicant further argues that at least sections b), c) and d) of applicant's sole independent claim 1 are not taught or suggested by the combined teaching of cited document (Page 13 of response filed on 12/20/2002).

The sections of b) to d) of claim 1 are directed to a method of diving a cell culture into two part (b), one part is used for the preparation of at least one production batch for production of at least one biological (c), and another part is used for a seed for the preparation of at least one subsequent preproduction batch.

Applicant does consider that the distinctiveness of presently claimed method is to divide the cells into two separate parts, one part for a production batch or batches and a second part for seed or a subsequent preproduction batch or batches.

In face, only section of b) recites the novelty that Applicants thought comprises to divide the cell culture into two parts, wherein the recitations of c) to d) just recite what the two divided parts used for. Sections e) and f) are all optional steps, and step f) is just directed to a repeated steps of b) to e). In this content, steps c) to e) are just an intended use of the procedures, which not add any more inventive steps of claimed method.

Griffith et al. do teach to inoculate cells and culture the cells into different paths, one is for harvesting the cells that product a biological and another is to maintain the cell culture as seed. It is so clear in this content that inoculation means culturing, and harvesting or passing cells means to prepare preproduction batch or seed. Therefore, theses limitations all taught by prior art.

While Griffith et al. does not explicitly mention to divide cells into two parts, or the ration of the first parts of cells populations is 80% to 90% and the second part as 10 to 20%, Griffith et al. do teach that the harvested cells are only from the seed of $1x10^5$ /ml or 2-3 X 10^5/ml cells to grow up to 1-2 $x10^6$/ml after 3-4 days culture, which meet the limitation of the 10 or 20% of the initial cells seed density and 80-90 % of final density of cells in preproduction batch.

Moreover, Grifffith et al. also teach on page 59 and 67, the cells in the scale-up culture can be harvested, diluted in the fresh medium and serum, and passaged on or after the growth phase, the cells can be harvested for a product (page 67). This product can be vaccine, interferon, and monoclonal antibody (page 59).

Therefore, it is obvious for any person with ordinary skill in the art, the procedure of dilution and passing cell lines means that the cells are used as a seed, and harvesting the cells after the growth phase for the product means that population of cells is used as a preproduction and production batch.

Although Griffith et al. do not teach to freeze the cells, Pollard teach the method of freezing cells –135 °C to -176 °C (See pages 3 and 6).

Therefore, it would have been obvious for a person with an ordinary skilled in the art to be motivated by the disclosures of Griffith et al. to establish a scale-up cell culture method by selecting 1 to 1 ratio split in order to get a biological without delay in the industry assembly line because the cells in 1 to 1 ration does not need to wait a long time to reach to a log phase, and further adapt a method taught by Pollard for freezing cells when massive culture of cells need to be frozen. As there is no unexpected result due to the 1 to 1 ration dividing, the rejection is still maintained.

New Ground of Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 contains the trademark/trade name cytodex-3. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe micro-carrier and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 7-22 and 26 are still rejected under 35 U.S.C. 102(b) as being anticipated by Griffiths et al. (Scale-Up of Suspension and Anchorage-dependent Animal Cells in Basic Cell Culture protocols, Edited by Pollard et al. Humana Press Inc, 1997, pp. 59-75).

Griffiths et al. teach several scale-up animal cell culture methods, which include the suspension cells and none-suspension cells culture methods. For the suspension cells, they teach a hollow-fiber cartridges method, Anchorage-dependent culture method in roller culture system or glass bead immobilized beds by using microcarrier cytodex 3 (pp. 67-71, section 3.2.1.3. and 3.2.2).While Griffith et al. do not use exactly same description of diving the cells of the preproduction batch into a first part and a second part, and employing said first part for preparation of production biological, and the second part as seed for preparation of at least one

subsequent preproduction batch, Griffith et al. do teach to inoculate cells from 1 or 2-3 $x10^5$/ml to reach to a log phase at concentration of 1 or 2 $x10^6$/ml, and harvest cells when they are used for producing a biological product (page 62-63 and 67) or dilute and change the cell medium for passing on the cell line. In this content, the cells harvested are considered as the first part of preproduction batch and the cells maintained and re-inoculated at a lower density are considered as a second part of seed for preparing the next preproduction batch. The biological products as taught by Griffith et al are vaccine, interferon, monoclonal antibody, and plasminogen activator etc. (pp. 59, 1st paragraph lines 1-9), in which the vaccine can be made by a mutated virus, the plasminogen activator is an enzyme to activate the plasminogen, and interferon is a protein. Because Griffith et al. teach that the harvested cells are only from the seed of $1x10^5$/ml or 2-3 X 10^5/ml cells to grow up to 1-2 $x10^6$/ml after 3-4 days culture (See page 63). Moreover, The Griffith et al. teach to use CHC cells (pp. 59, 1st paragraph, lines 1-18), and detach the cells with trypsin/EDTA (pp. 67, step 6 and pp. 71, step 7). Trypsin is a proteolytic enzyme. In addition, Griffths et al. teach that at the begging of the culture, the cell population is 1 or 2-3 $x10^5$/ml cells and the final cells density is at 1-2 $x10^6$/ml. The population of 1 or 2 $x10^5$/ml cells is just about 10% or 20% of $1x10^6$/ml of final concentration of preproduction cells (page 63). In face, the recitations of c) to d) of claim 1 just recite what the two divided parts used for. Step e) and f) are all optional steps, and step f) is just directed to a repeated steps of b) to e)., wherein steps c) to e) are just an intended use of the procedures, which not add any more inventive steps of claimed method. Therefore, the disclosures of Griffith et al. anticipate the rejected claims.

Claims 1-2, 10, 16, 17, 18, 22, and 25-26 are still rejected under 35 U.S.C. 102(b) as being anticipated by Pollard (Basic Cell Culture Protocols, Edited by Pollard et al. Humana Press Inc., 1997, Step 14-20 on page 3 and Section 3.2 on page 4-5)

Pollard teaches a method for maintenance and subculture of transformed CHO-S cell line (claim 26). The method comprises rapidly defrost the frozen cells from –135 or –176 ° at 37°C and remove the frozen medium by centrifugation, resuspend the cells in a prewarm medium and place the cells suspension in a cell culture incubator for 2 days. After 2 days, the cells reached to a confluence are trypsinized, and resuspended as a single cell suspension. An aliquot of 10% of total cell suspension (The first part of preproduction batch) are added into a new tissue culture

vessel for culturing to a confluence, which is then used for a massive culture of producing a biological. Some subculture of cells is maintained (second part of seed) in the incubator for the next subculture (repeat the steps of subculture). In this content, some cell populations in subculture are used as preproduction batch and some of them are used as seed for preparation of next preproduction batch or seed. The subculture is to divide cells into different purposes of cultures. Pollard also teaches that the subculture of cells can be a mass-culture. Once the mass culture is obtained, it also can be frozen in a large number of vials to provide a base of future experiments (page 6-7). The cells are frozen the cell lines at –135 or –176 ° (page 3). In face, the recitations of c) to d) of claim 1 just recite what the two divided parts used for. Step e) and f) are all optional steps, and step f) is just directed to a repeated steps of b) to e)., wherein steps c) to e) are just an intended use of the procedures, which not add any more inventive steps of claimed method. Therefore, the claimed invention is anticipated by the cited prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li

April 19, 2004

JAMES HOUSEL 4/19/04
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